

Serum Urea and Serum Creatinine in Patients with Type-2 Diabetes Mellitus and their Prognostic Role as Effective Renal Markers in Type-2 Diabetes

Romy. W. Marshnil¹, Archana Mony², Ganesh G³, Aaron Vetha Jose J^{4*}

¹MD, Associate professor, Department of Biochemistry, Government Thoothukudi Medical College, Tamil Nadu, India

²MD, Assistant Professor, Department of Biochemistry, Kanyakumari Government Medical College, Asaripallam, Nagercoil, Tamil Nadu, India

³MD, Associate Professor, Department of Biochemistry, Government Namakkal Medical College, Tamil Nadu, India

⁴MD, Assistant Professor, Department of Biochemistry, Kanyakumari Govt. Medical College, Asaripallam, Nagercoil 629201, Kanyakumari District, Tamilnadu - India

Received: 25-08-2023 / Revised: 28-09-2023 / Accepted: 30-10-2023

Corresponding author: Dr. Aaron Vetha Jose J

Conflict of interest: Nil

Abstract:

Context: Type 2 diabetes mellitus is the leading risk factor for impaired renal function, and approximately 20 to 30% of diabetic patients progress to diabetic nephropathy.

Objective: This study was conducted to study the relationship between blood glucose, serum urea and serum creatinine levels in diabetic patients and non-diabetic healthy individuals, so as to find out the prognostic role of serum urea and creatinine as effective renal markers in type-2 diabetic patients.

Materials and Methods: The study group consisted of 100 patients with type-2 diabetes and 100- nondiabetic healthy controls. Fasting and Post Prandial blood sugar, serum urea and serum creatinine were assayed. Data was analysed using student's 't' test and linear regression analysis.

Results: There was a statistically significant increase in the serum urea ($p < 0.001$) and creatinine levels ($p < 0.05$) in diabetic patients. Also, there was a statistically significant difference ($p < 0.001$) observed in diabetic patients with increasing duration of diabetes and with associated diabetic complications.

Conclusion: Good glycemic control, along with routine monitoring of serum urea and creatinine levels is absolutely needed in diabetic patients to prevent progressive renal impairment.

Keywords: Blood Glucose, Diabetic Nephropathy, Glycemic Control, Type 2 Diabetes Mellitus.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Diabetes mellitus is one of the most common non-communicable diseases in the world. By the year 2030, about 350 million people all over the world are likely to be affected with Diabetes mellitus [1]. The prevalence of diabetes has steadily increased over the past ten years, especially in developing countries like India [2]. India is one of the six countries in the South East Asian region with more than 82 million diabetic patients, and this number is expected to increase to around 151 million diabetic patients by the year 2045 [3].

Uncontrolled diabetes can lead on to cardiovascular, renal, neurological and retinal complications. Among these, diabetic nephropathy is the most common complication of type-2 diabetes. Diabetic nephropathy is the most common cause for renal failure, accounting for nearly 44 percent of new cases [4]. Hence, it is important to detect diabetic

nephropathy earlier, so as to prevent development of end stage renal failure [5]. Diabetic nephropathy is characterised by microalbuminuria with excretion of proteins-especially albumin of more than 300 mg per day and also along with abnormality in serum urea and creatinine levels. In diabetic nephropathy, serum urea and creatinine are usually elevated, along with raised blood glucose levels in uncontrolled diabetes, which correlates with the severity of kidney damage.

Urea is the major nitrogenous end product of protein metabolism in humans. It is excreted in the urine by the kidneys [6]. Creatinine is formed from creatine phosphate by a non-enzymatic spontaneous reaction in the muscle. Creatinine is excreted in the urine at a constant rate [7,8]. Creatinine level in the serum is a sensitive indicator of renal function [9]. Serum urea and serum creatinine are the best biochemical

markers in determining the prognosis, progression and initiating dietary restriction in renal disease in patients with type 2 diabetes mellitus [10]. Thus, measurement of serum urea and creatinine are easily available tests which can assist in early detection and prevention of diabetic nephropathy and limit the progression to end stage renal disease [11].

Thus, this study aims to evaluate the levels of serum urea and creatinine in diabetic patients and compare these values with non-diabetic healthy individuals, so as to study the variation in serum urea and serum creatinine levels in relation to blood sugar levels, duration of diabetes, associated diabetic complications and prolonged treatment for diabetes.

Materials and methods

Study design

This case-control study was done in a tertiary care medical college hospital in South India. A prior permission from the institutional human ethical committee of the medical college-hospital was obtained before conducting the study. Both oral as well as written informed consent was obtained from all the study participants before enrolling them in the study.

For this study, 100 known cases of type-2 diabetes were recruited from the OP and wards of the department of general medicine of the hospital. The age group of the study participants ranged from 40-70 years. Another group consisting of 100, age and sex matched normal healthy individuals without diabetes formed the controls.

All the study participants were recruited into the study after considering suitable inclusion and exclusion criteria. After separation of serum from the clot, the serum samples were processed in a fully automated clinical chemistry analyser.

Fasting blood sample was used for fasting blood sugar determination and post prandial blood sample was used for post prandial blood sugar analysis. Both the fasting and post prandial blood glucose were determined by Glucose-Oxidase-Peroxidase enzymatic kit method.

Serum urea was analysed by Urease-GLDH method using enzymatic reagent kit. Serum creatinine was estimated by modified Jaffe's method using enzyme kit.

Table 1: Mean values of serum urea, serum creatinine, Fasting and Post prandial blood sugar levels in type 2 diabetic patients compared to non-diabetic healthy controls.

Investigations	Patients with type-2 Diabetes (mean \pm SD)	Non-diabetic healthy controls (mean \pm SD)	P-value
Serum Urea mg/dl	39.36 \pm 10.087	27.10 \pm 5.056	0.000**
Serum Creatinine mg/dl	1.339 \pm 0.7893	1.024 \pm 0.2600	0.007*
FBS mg/dl	208.1 \pm 68.82	89.02 \pm 6.65	0.000**
PPBS mg/dl	268.5 \pm 67.52	120.75 \pm 9.36	0.000**

** - Highly Significant ($p < 0.001$), * - Significant ($p < 0.05$), FBS - Fasting Blood Sugar; PPBS-Post Prandial Blood Sugar.

Statistical analysis

Statistical analysis was done using SPSS software, statistical package version 21.0. Results were expressed as mean \pm SD. Students't'- test, Chisquare test and linear regression analysis were used to compare the results among the diabetic and non-diabetic group. Statistically significant difference was considered when p value was less than 0.05.

Results

In this study, the mean values of serum urea, serum creatinine, fasting and post prandial blood sugar values were compared between type-2 diabetic patients and non-diabetic healthy people, and it was shown in (Table 1). A highly statistically significant increase with ($p < 0.001$) was found in serum urea values and a statistically significant difference in serum creatinine values with ($p < 0.05$) was observed in diabetic patients. To study the association between blood sugar levels with serum urea and serum creatinine in type -2 diabetic patients, a Pearsons' correlation was performed, which was shown in (Figure 1a, 1b, 1c). It shows a significant positive correlation between blood sugar values with serum urea and serum creatinine values in diabetic patients.

The influence of age, sex and prolonged duration of diabetes on serum urea and serum creatinine in type-2 diabetic patients was shown in (Table 2). There was no statistically significant effect of age and sex on serum urea and serum creatinine levels in diabetic patients. But there was a highly statistically significant effect of prolonged duration of diabetes ($p < 0.001$) on serum urea and serum creatinine levels in type-2 diabetic patients. The influence of diabetic complications and prolonged treatment for diabetes by various treatment methods on serum urea and serum creatinine levels in diabetic patients were shown in (Table 3).

There was a statistically significant increase in serum urea and serum creatinine values ($p < 0.001$) due to associated diabetic complications and prolonged treatment for diabetes in diabetic patients. (Figure 2) shows the comparison of duration of diabetes, associated diabetic complications and prolonged treatment for diabetes with serum urea and serum creatinine values in type-2 diabetic patients.

Table 2: Influence of age, sex and duration of Diabetes on serum urea and serum creatinine values in type-2 diabetic patients

Age		Serum Urea		Serum Creatinine	
		Mean±SD	P-value	Mean±SD	P-value
	> 56 years	40.92±10.749	0.131	1.469±0.9044	0.106
	≤ 56 years	37.86±9.267		1.214±0.6447	
Sex	male	39.02±10.444	0.738	1.392±0.9510	0.505
	female	39.70±9.811		1.286±0.5904	
Duration of diabetes	< 10 years	27.1±5.05	0.000**	1.024±0.259	0.000**
	> 10 years	49±12.316		2.085±1.32	

** - Highly Significant (p < 0.001), * - Significant (p < 0.05)

Table 3: Effect of associated diabetic complications and prolonged treatment for diabetes by various treatment methods on the levels of serum urea and serum creatinine in type-2 diabetic patients

		Serum Urea		Serum Creatinine	
		Mean±SD	P-value	Mean±SD	P-value
Associated Diabetic complications	Yes	46.09±10.223	0.000**	1.768±1.0074	0.000**
	No	34.07±6.060		1.002±0.2548	
Various treatment methods for Diabetes	Insulin	53.00±7.703	0.000**	2.200±1.0708	0.000**
	OHA+Insulin	48.87±13.032		2.113±1.4367	
	OHA	36.79±7.806		1.144±0.4212	

** - Highly Significant (p < 0.001), * - Significant (p < 0.05), OHA- Oral Hypoglycemic Agents.

List of Figures

Figure 1a:

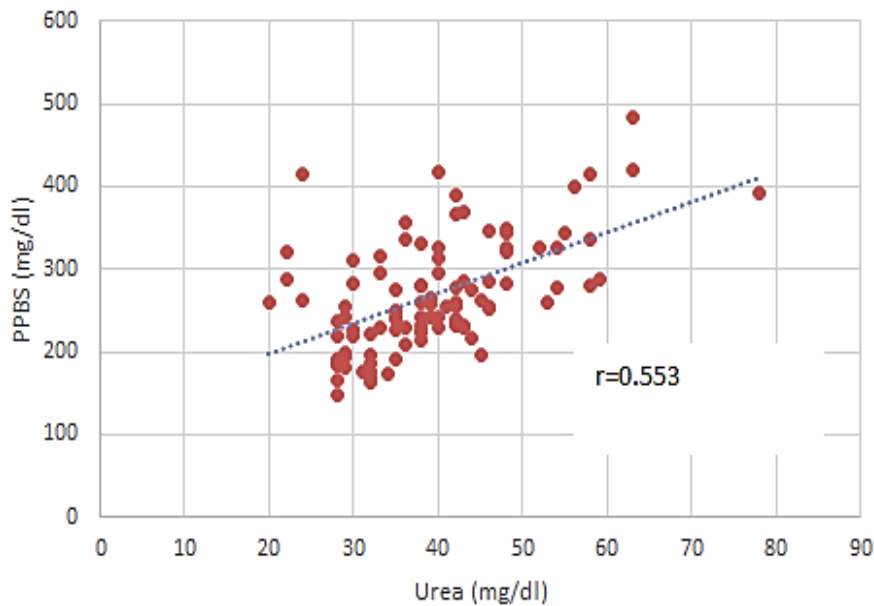


Figure 1b:

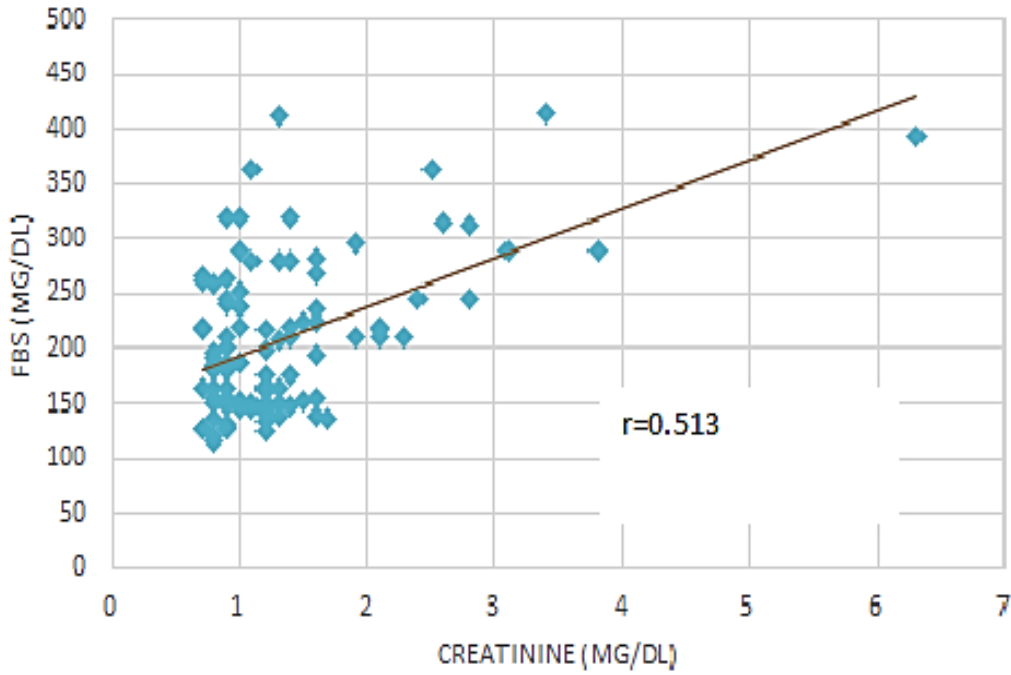


Figure 1c

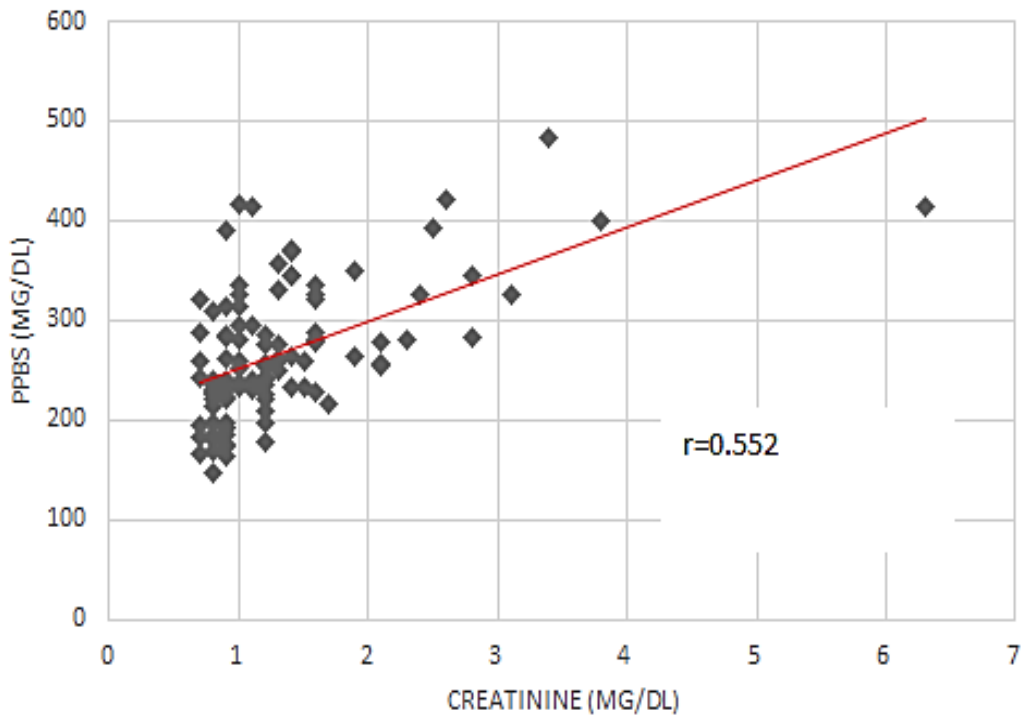


Figure 1a, 1b, 1c: Scatter diagrams showing positive correlation between blood sugar levels with serum urea and serum creatinine in diabetic patients

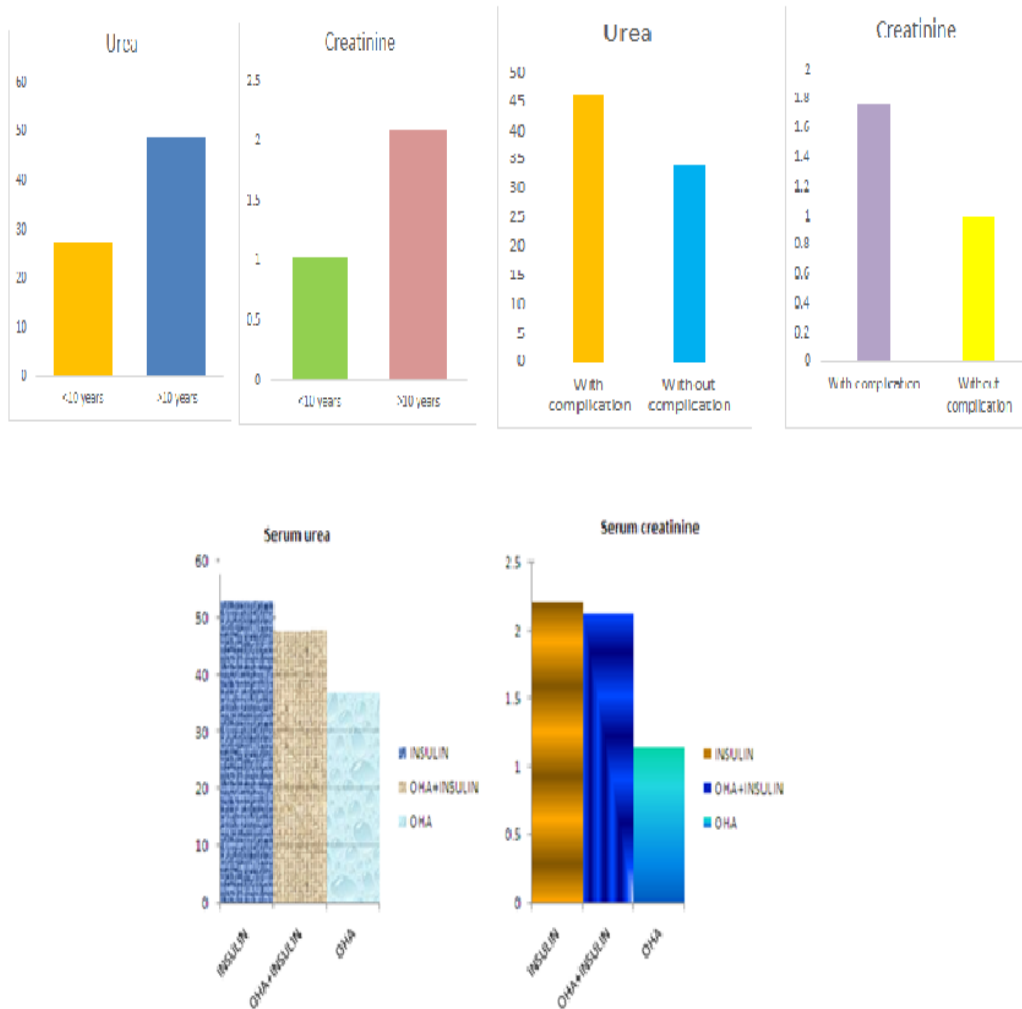


Figure 2: Bar diagrams showing comparison of prolonged duration of diabetes, associated diabetic complications and prolonged treatment for diabetes by various treatment methods with serum urea and creatinine values in type-2 diabetic patients

Discussion

Uncontrolled diabetes is the major cause for increased morbidity and mortality due to renal failure [12]. Diabetic nephropathy occurs in about one-third of people with type-2 diabetes and is in increasing trend [13]. Though the incidence of diabetic nephropathy was considered substantially higher in type-1 diabetes [14], recent data suggest that risk for development of renal failure is equal in both type-1 and type-2 diabetes [15]. Though there have been many studies on microalbuminuria and diabetic nephropathy [16,17], the role of serum urea and serum creatinine tests in patients with type-2 diabetes mellitus and their correlation with blood sugar levels has not yet been reported. In the present study, we have compared serum urea and serum creatinine levels in patients with type-2 diabetes mellitus against non-diabetic healthy controls. We have also studied the influence of age, sex, duration

of diabetes, associated diabetic complications and prolonged treatment for diabetes on the levels of serum urea and serum creatinine in diabetic patients.

In this study, there was a statistically significant increase with (p<0.001) and (p<0.05) in serum urea and serum creatinine levels respectively in type-2 diabetic patients when compared to healthy non-diabetic controls. The findings in our study was in accordance with another study done by [18], who also showed statistically significant increase in levels of serum urea and serum creatinine in diabetic population. In our study, the levels of serum urea and serum creatinine when correlated with blood sugar values in type -2 diabetic patients by Pearsons' correlation, showed a significant positive correlation of serum urea and serum creatinine with blood sugar levels. Our study shows that, uncontrolled diabetes with poorly controlled blood sugar levels causes a significant increase in serum urea and serum

creatinine levels and greatly increases the risk of aggravating diabetic nephropathy leading to renal failure in diabetes. The results in our study were similar to another study done by [19], which also showed statistically significant correlation between blood sugar levels and serum urea and serum creatinine in type-2 diabetic patients.

In our study, there was no statistically significant effect of age and sex on serum urea and serum creatinine levels in type-2 diabetic patients. These findings were in contrast to a study done by [20], which showed that, serum urea and serum creatinine increased with advancing age in diabetes and it was due to age related degenerative changes in the nephrons of the kidney. But similar to our study, no statistically significant difference was observed in serum urea and serum creatinine levels among diabetic males and females.

In the present study, there was a statistically significant effect of prolonged duration of diabetes ($p < 0.001$) on serum urea and serum creatinine levels in type-2 diabetic patients. Another study done by [21] has shown increase in fasting blood glucose, serum urea and serum creatinine levels with increasing duration of diabetes. The increase in serum urea and serum creatinine levels with increasing duration of diabetes in our study could be attributed to reduction in filtration capacity of the kidneys with prolonged duration of uncontrolled hyperglycemia. Over time, high blood sugar levels, if left uncontrolled, damages the kidney nephrons, thus leading to increase in serum urea and serum creatinine levels with progressive loss of renal function.

In our study, we have also found a statistically significant increase in serum urea and serum creatinine levels ($p < 0.001$) with associated diabetic complications and prolonged treatment by various treatment methods for uncontrolled diabetes.

A study done by [22] has shown a statistically significant increase in serum urea and serum creatinine levels in diabetic patients with associated diabetic complications like cardiovascular diseases, hypertension, with risk factors like alcohol drinking and cigarette smoking. Associated diabetic complications with uncontrolled hyperglycemia in diabetes, significantly increases the renal damage in diabetes.

Conclusions

Serum urea and serum creatinine are the best biochemical indicators for assessing renal function in diabetic patients. Increase in duration of diabetes, along with poor blood glucose control affects the renal function and leads to early renal impairment in diabetic patients. Hence, we recommend regular and vigilant monitoring of serum urea and serum creatinine, along with blood sugar levels in diabetic

patients, so as to prevent progression of Diabetes mellitus to Diabetic nephropathy and renal failure.

Acknowledgements: The authors of this study are thankful to all the study participants who actively participated in the above study.

References

1. Yach D, Stucker D, Brownell KD. Epidemiologic and economic consequences of global epidemics of obesity and diabetes. *Nat Med*, 2006;12:62-6.
2. Bamanikar SA, Bamanikar AA, Arora A. Study of serum urea and creatinine in diabetic and non-diabetic patients in a tertiary teaching hospital. *J Med Res*, 2016;2(1):12-5.
3. Kaveeshwar S. The current state of diabetes mellitus in India. *Australasian Med J*, 2014;7(1):45-8.
4. Pradeep KD. Renal function in diabetic nephropathy. *World J Diabetes*, 2010;1(2):48-56.
5. Mishra KP, Mawar A, Kare P, Verma N. Relationship between fasting blood glucose, serum urea, serum creatinine and duration of diabetes in type-2 diabetic. *Flora Fauna*, 2015;21:127-32.
6. Salazar, Jose H. Overview of urea and creatinine. *Lab Med*, 45(1):19-20.
7. Schrier RW, Gottschalk CW. Diseases of the kidney. Boston, University of Chicago: Little, Brown Publishers, 1993;2:153-89.
8. Baxmann AC, Ahmed MS, Marques NC, Menon VB, Pereira AB, et al. Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin c. *Clin J Am Soc Nephrol*, 2008;3(2):348-54.
9. Deepa K, Goud MBK, Devi OS, Devaki R, Nayal B, Prabhu, et al. Serum urea, creatinine in relation to fasting plasma glucose levels in type 2 diabetes. *IJPBS*, 2011;1:279-83.
10. Shlomo M, Polonsky KS, Larsen PR, Kroenberg HM. Diabetes Mellitus. Williams Textbook of endocrinology. Philadelphia: Elsevier, Saunders Publishers, 2011;1371-435.
11. Shrestha S, Gyawali P, Shrestha R, Poudel B, Sigdel M, Regmi P, et al. Serum urea and creatinine in diabetic and non-diabetic subjects. *JNAMLS*, 2008;9:11-2.
12. Singh P, Khan S, Mittal RK. Renal function test on the basis of serum creatinine and urea in type-2 diabetics and non-diabetics. *Bali Med J*, 2014;3(1):11-4.
13. Rehman G, Khan SA, Hamayun M. Studies on diabetic nephropathy and secondary disease in type 2 diabetics. *Int J Diab Dev Countries*, 2005;25:25-9.
14. Cowie CC, Port FK, Wolfe RA, Savage PJ, Moll PP, Hawthorne VM. Disparities in incidence of diabetic end-stage renal disease

- according to race and type of diabetes. *N Engl J Med*, 1983;321(16):1074-9.
15. Inassi J, Vijayalakshmy R. Role of duration of diabetes in the development of nephropathy in type 2 diabetic patients. *Natl J Med Res*, 2013;1(2):5-8.
 16. Mandal FK, Jyothrimayi D. Comparative study of microalbuminuria and glycated haemoglobin levels in type 2 diabetic complications. *Asian J Pharm Clin Res*, 2016;8(2):356-60.
 17. Singh P, Khan S, Mittal RK. Glycemic status and renal function among type-2 diabetics. *Bangladesh J Med Sci*, 2014;13(4):406-10.
 18. Kanwar G, Jain N, Sharma N, Shekhawat M, Ahmed J, Kabra R. Significance of serum urea and creatinine levels in type 2 diabetic patients. *IOSR-JDMS*, 2015;14(8):65-7.
 19. Idonije BO, Festus O, Oluba OM. Plasma glucose, creatinine and urea levels in type 2 diabetic patients attending a nigerian teaching hospital. *RJMS*, 2011;5:1-3.
 20. Amer M Hussin, Hayder T Al-zubaidi, Zainab J Abdulameer, Husham Abdlstar Abdlkarem. the relationship between serum creatinine, serum urea and blood sugar of patients in Diyala city in Iraq. *European J of molecular and cellular medicine*, 2020;7(3):485-93.
 21. Mishra KP, Mawar A, Pawan K Kare, Verma N. Relationship between fasting blood glucose, serum urea, serum creatinine and duration of diabetes in type 2 diabetic patients. *Flora and Fauna*, 2015;21(1):127-32.
 22. Kene K, Wondimnew T, Welde M, Mateos T, Adugna T, Gerema U, et al. Prevalence and determinants of impaired serum creatinine and urea among type 2 diabetic patients of jimma medical center, Jimma, Southwestern Ethiopia, 2019. *Endocrine and Metabolic Science*, 2021;3:1-7.